REMARKS

Claims 1-23 are pending in the application. Applicants have amended several claims and added new claims 24-26 without introducing new matter. Claim 3 has been canceled without prejudice and without disclaimer of the subject matter contained therein. Claims 1,2 and 4-26 are pending.

The claims have been amended to indicate that the previously recited complexing agent is a cyclic oligosaccharide as set out in original claim 3. New claims 24-26 find clear support in the specification. With regard to new claim 24, support for the formation of low-energy bonds is found on page 7 at lines 6-9. The stabilizing agent and/or surfactant of new claim 25 is found on page 11, at lines 10-18. The antiviral nature of the active ingredient, claimed in new claim 26, is supported generally throughout the specification in the discussions concerning the wide range of potential active ingredients.

35 U.S.C. § 102

Claims 1, 2, 6-8, 12, 13, 21 and 22 stand rejected under 35 U.S.C.§ 102(e) as anticipated by U.S. Patent No. 5,641,515 to Ramtoola.

The subject matter of claim 3, which was not subject to rejection over Ramtoola has been incorporated into the independent claims. Accordingly, the rejection is moot. For completeness, however, Ramtoola is discussed below.

Ramtoola '515 discloses a controlled release pharmaceutical formulation comprising nanoparticles formed of a biodegradable polycyanoacrylate polymer in which insulin is entrapped. The Office Action indicates that although Ramtoola does not specifically teach a separate complexing agent in addition to the polymer, it is the position of the examiner that nothing in applicant's claim language prevents the polymer from acting as the complexing

agent. Applicants respectfully submit that independent claim 1 now clearly requires at least one polymer, at least one active ingredient, and, in addition, a cyclic oligosaccharide as the complexing agent. Ramtoola simply does not teach or suggest this three component system and the cyclic oligosaccharide. Rather, Ramtoola relies upon the polymer to perform dual duty as both the polymer and the complexing agent.

Accordingly, Ramtoola '515 does not teach or suggest each claimed element. Applicants respectfully submit, that in light of the amendments to the claims, Ramtoola '515 does not teach or suggest the nanoparticles or the method for preparing them as claimed. Withdrawal of the 35 U.S.C. § 102 rejection is respectively requested.

35 U.S.C. § 103

Claims 1, 2, and 6 - 23 stand rejected under 35 U.S.C. § 103(a) as being obvious over Ramtoola '515. As discussed above, the rejection is moot and Ramtoola '515 simply does not teach or suggest the claimed nanoparticles including each of a polymer, an active ingredient, and additional complexing agent, specifically a cyclic oligosaccharide. The office action indicates that any well known drug would benefit from control and release properties and, therefore, would be obvious to include in the claimed invention. Assuming, arguendo, that this is true, Ramtoola '515 still does not teach the claimed nanoparticles, or methods of making them, which include at least one active ingredient, a polymer, and a cyclic oligosaccharide, as claimed. Accordingly, Ramtoola '515 does not teach or suggest the claimed invention. Withdrawal of the 35 U.S.C. § 103 obvious rejection over Ramtoola '515 is respectfully requested.

Claims 1 - 5 stand rejected under 35 U.S.C. § 103(a) as being obvious over the hypothetical combination of US Patent No. 5,932,248 (Chen et al.) with US Patent No.

5,246,611 (Trinh). Chen et al. discloses a controlled release preparation comprising anionic polymer matrix loaded with an active compound. The active compound is complexed with a complexing agent such as a metal ion to modify the release of the active compound from the polymer matrix.

Chen et al. seeks to solve the problem of the " burst release effect ". This effect is frequently observed when matrices with a high drug loading release the drug rapidly and is a result of weak bonding or superficial location of drug during the formulation of the high loading matrix, as disclosed column 1, lines 59-67. Thus, the invention disclosed in Chen et al. develops a biodegradable ionic polymer as the matrix and implements an ionic interaction as the drug-polymer binding mechanism (column 2, lines 45-55).

We respectfully submit that Chen et al. is inapplicable since it is directed to combinations of DOX-metal ion and DOX-metal ion-polymer complexes. Chen et al. at Column 4, lines 3 - 8 clearly sets forth this distinction as follows:

> In this regard, it should be noted that the present invention is not directed to the controlled release of DOX-iron, but rather the use of the formation of DOX-metal ion and DOX-metal ion-polymer complexes as a control release mechanism to provide a system with optimum/desirable release of native DOX.

Applicants claimed invention specifies that each nanoparticle comprises a polymer, at least one active ingredient and, in addition, a cyclic oligosaccharide. The claimed nanoparticles do not include complexes of the active ingredient and complexing agent, without a polymer in combination with complexes of the active ingredient, complexing agent, and a polymer as taught by Chen et al. Such a combination defeats the purpose of applicants' invention. Accordingly, Chen et al. does not render the claimed nanoparticles obvious.

Trinh is cited to introduce the use of cyclodextrin complexes as the complexing agent. However, Trinh does not overcome the basic deficiency of Chen et al. as discussed above, with respect to the use of both DOX-metal ion and DOX -metal ion-polymer complexes rather than the claimed polymer-active ingredient-complexing agent complex as claimed herein. Accordingly, the hypothetical combination of Chen et al. with Trinh still does not teach or suggest the claimed invention.

Likewise, Trinh contains no teaching or suggestion to motivate one skilled in the art to replace the complexing ionic agent in the compounds disclosed by Chen et al. with a cyclic oligosaccharide, since the complexes form low-energy chemical bonds rather than ionic interactions between the active ingredient and the cyclic oligosaccharide.

Accordingly, applicants respectfully request withdrawal of the 35 U.S.C. § 103 rejection based on Chen et al. in view of Trinh '611.

Applicants respectfully submit that all pending claims are now in condition for allowance and clearly distinguishable over the prior art of record. Accordingly, early reconsideration and allowance of all pending claims is respectfully request.

Respectfully submitted,

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Version with Markings to Show Changes Made to the Claims

Please amend the claims as follows:

1) (Twice Amended) Nanoparticles comprising:

at least one polymer;

at least one active ingredient; and

at least one cyclic oligosaccharide ~~compound able to complex said active ingredient, said nanoparticles having a size between about 40 and about 300 nm~~.

Please cancel claim 3 without prejudice and without disclaimer of the subject matter contained therein.

4) (Amended) The nanoparticles according to Claim 1, wherein the ~~compound able to complex the active ingredient~~ cyclic oligosaccharide is a neutral or charged, native, branched or polymerized or chemically modified cyclodextrin.

5) (Amended) The nanoparticles according to Claim 1, wherein the ~~compound able to complex the active ingredient~~ cyclic oligosaccharide is a cyclodextrin chemically modified by substitution of one or more hydroxypropyls by alkyl, aryl, arylalkyl, glycosidic groups, or by etherification, esterification with alcohols or aliphatic acids.

13) (Amended) The nanoparticles according to Claim 1, wherein the proportion of ~~compound able to complex the active ingredient~~ cyclic oligosaccharide is from about 0.1 to about 70% by weight of the weight of the nanoparticles.

14) (Twice Amended) A method of preparing nanoparticles according to Claim 1, comprising:

a) preparing a complex of the at least one active ingredient with the at least ~~one compound able to complex said active ingredient~~ cyclic oligosaccharide in solution in an aqueous or non-aqueous solvent,

b) adding at least one monomer of the polymer in the solution obtained at step (a), and

c) polymerizing the monomer, optionally, in the presence of one or more of a surfactant and/or stabilising agent.

15) (Amended) A method for preparing nanoparticles according to Claim 1, comprising:

a) preparing nanoparticles by forming an inclusion complex of a poly(alkyl-cyanoacrylate) polymer, and a ~~compound able to complex an active ingredient~~ cylic oligosaccharide; and

b) associating the active ingredient with the nanoparticles.

16) (Twice Amended) The method for preparing nanoparticles according to Claim 15, further comprising:

a) preparing a solution of at least one ~~compound able to complex an active ingredient~~ cyclic oligosaccharide in an aqueous or non-aqueous solvent;

b) gradually adding at least an alkylcyanoacrylate monomer, to the solution of step (a);

c) polymerizing the monomer in the presence of one or more of a surfactant and/or stabilising agent; and

d) after control and optional purification of the nanoparticles obtained at step (c), incubating the nanoparticles in a solution of active ingredient in an aqueous or non-aqueous solvent.

18) (Twice Amended) The method according to Claim 14, wherein, at steps (a), (b) and (d), the solvent is selected such that, while maintaining conditions of polymerization of the polymers, the solubility of the active ingredient and of the ~~compound able to complex said active ingredient~~ cyclic oligosaccharide is maintained at a maximum.

19) (Amended) The method according to Claim ~~14~~ 16, wherein step (c) is conducted with no surfactant and/or stabilising agent.

20) (Amended) The method according to Claim 14, wherein, at step (a) the proportion of ~~compound able to complex the active ingredient~~ cyclic oligosaccharide is from about 0.1 to about 70 % by weight relative to said active ingredient.

21) (Amended) A medicinal product with targeted effect and improved therapeutic index produced by the method according to Claim ~~14~~ 16.

22) (Amended) Nanoparticles obtained by the method according to Claim ~~16~~ 18.

23) (Amended) Nanoparticles according to Claim 22, wherein the ~~compound able to complex an active ingredient~~ cyclic oligosaccharide is selected from the group consisting of

a neutral, a charged, a native, a branched, a polymerized, and a chemically modified cyclodextrin.

Please add the following new claims

24) The nanoparticles according to claim 1, wherein the active ingredient combines itself with one or more cyclic oligosaccharides through the creation of low-energy chemical bonds.

25) The nanoparticles according to claim 1, wherein said nanoparticles further comprise a stabilizing and/or surfactant agent.

26) The nanoparticles according to claim 1, wherein the active ingredient is an antiviral.